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10/583,089	06/15/2006	Andreas Nandy	MERCK-3178	8804

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EXAMINER	
ROONEY, NORA MAUREEN	
ART UNIT	PAPER NUMBER
1644	

NOTIFICATION DATE	DELIVERY MODE
03/29/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

docketing@mwzb.com

Office Action Summary	Application No.	Applicant(s)	
	10/583,089	NANDY ET AL.	
	Examiner	Art Unit	
	NORA M. ROONEY	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 February 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,12-17 and 21-24* is/are pending in the application.

4a) Of the above claim(s) *1-9 and 14-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10, 12-13, 21-22, 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 02/03/2010 has been entered.

2. Claims 1-10, 12-17 and 21-24 are pending.

3. Claims 1-9 and 14-17 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Groups, and claim 23 is withdrawn from consideration as being directed to a non-elected species there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 08/19/2008. It is noted that Applicant elected the species of SEQ ID NO:2 with or without the signal peptide. Claim 23, which is directed to variant polypeptides with one or more cysteine residues replaced with any amino acid reads on many different polypeptides and is not encompassed by the elected species.

4. Upon further consideration, the Examiner has extended the search to include the species of SEQ ID NO:4 in addition to the elected species of SEQ ID NO:2. SEQ ID NO:2 was elected in the response filed on 08/19/2008.

5. Claims 10, 12-13, 21-22 and 24 are currently under examination as they read on the polypeptide of SEQ ID NO 2 or SEQ ID NO:4 with or without their signal sequences and a pharmaceutical composition thereof.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 10, 21-22 and 24 are rejected are rejected under 35 U.S.C. 102(b) as being anticipated by Gavrovic et al. (PTO-892 mailed on 11/28/2008; Reference V) as evidenced by the specification on page 4, lines 1 and 19-22 for the same reasons as set forth in the Office Action mailed on 11/05/2009.

Gavrovic et al. teaches the isolated Sec c 4 protein from *Secale cereale* having a molecular weight of about 55-60 kDa and a pI in the range of 9.2 to 9.7 (In particular, abstract).

The specification on page 4 teaches that Sec c 4 is the Group 4 allergen isolated from *Secale cereale* having the amino acid sequence of SEQ ID NO: 2 or SEQ ID NO:4. The reference teaches the same isolated allergen from the same source, so the resulting allergen must necessarily have the sequence of SEQ ID NO:2 or SEQ ID NO:4.

Claims 10, 21-22 and 24 are included in this rejection because the recitations of: the sequence set forth in SEQ ID NO:2 or 4 or encoded by the sequence set forth in SEQ ID NO 1 or 3 in claim 10; and a polypeptide comprising SEQ ID NO: 2 or 4, a polypeptide comprising amino acids 23 to 518 of SEQ ID NO:2, a polypeptide comprising amino acids 23 to 520 of SEQ ID NO:4 or a polypeptide encoded by the sequence set forth in SEQ ID NO 1 or 3 in claim 24 add no patentable weight. Determining the sequence of the reference allergen is merely further characterization of a known compound. Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999)"Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art... However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer. "The Court further held that "this same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art".

The "comprising" language in the claim 24 parts (b) and (d) open up those parts of the claim to read on full-length SEQ ID NO:2 and SEQ ID NO:4.

Claim 21 is included in this rejection because the patentability of a product does not depend on its method of production. In re Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985) See MPEP 2113. Further, once a product is fully disclosed in the art, future claims to that same product are precluded, even if that product is claimed as made by a new process.

The reference teachings anticipate the claimed invention.

Applicant's arguments filed on 02/03/2010 have been fully considered, but are not found persuasive.

Applicant argues:

"Gavorovic fails to teach *Secale cereale* c 4 allergens of the present application and fragments thereof

Applicants have reviewed the structural information of the instantly claimed molecules which range from -520 amino acids for the complete allergens and -497 amino acids for the claimed fragments. Applicants have performed *apriori* calculation of the molecular weight (MW) and isoelectric points (pI) of the polypeptides using Compute pI/MW, a program freely available from the Expert Protein Analysis System (EXPASY). The results of the computation are presented in the table below. It should be noted that all the N-terminal signal processed polypeptides of the instant invention, as recited in instant claim 24, are structurally different from Gavorovic's *Secale cereale* allergen. For example, with respect to the processed fragment of SEQ ID NO: 2 recited in claim 11, Compute pI/MW predicts that the theoretical value for the sequence (496 amino acids) is a pI of 9.10 and a MW of 54931.15 daltons. Both values are outside of what is taught by Gavrovic (i.e., MW of 55-60 kDa and pI of 9.2-9.7). As such, the polypeptides recited in (b), (d), (f), (h), and (j) of claim 24 are novel over what is taught by Gavorovic."

"Applicants submit that at least the mature polypeptides having the sequence set forth in SEQ ID NO: 2, 8, and 10 have different physiochemical characteristics from Gavorovic's polypeptides. This is because the iso-dectric (pI) value of each of the aforementioned mature proteins, which is dependent on the amino acid composition of the polypeptide chain, is different from what is taught by the cited reference. Accordingly, the mature proteins recited in claim 24 (a), 24 (g) and 24 (i) are novel over Gavorovic's disclosure. Withdrawal of the rejection is respectfully
requested.

With respect to the *Secale cereale* c 4 allergen of SEQ ID NO: 4 [see claim 24 (c)], Applicants submit that the PTO has not established that Gavorovic's polypeptides are structurally and/or functionally identical to the polypeptide(s) claimed herein. Absent such, the reference cannot anticipate what is claimed herein. For example, posted below are results of the search report carried out on June 16, 2008, which was used in the non-final rejection mailed November 28, 2008."

In the analysis which follows the aforementioned table, it is further acknowledged that among these top-matching sequences, *osly* AEB28051 (GenBank accession: AJ862830; GI:55859453; which encodes a protein of 518 amino acids) is identical to the instantly claimed polynucleotide of SEQ ID NO: 1. A second *Secale cereale* polynudeotide having ID AEB28053 (GI: 55859455; result 5) exhibited 81.2% identity to the claimed polynucleotide of SEQ ID NO: 1. A search on NCBI database with the GI accession numbers indicates that the reference sequences encode proteins having GenBank accession Nos. CAH92627 and CAH92630, respectively (see enclosed printouts). The PTO search report further indicates that the reference polynucleotides are disclosed in WO2005-059136 to Feibig et al. Coincidentally, WO 2005-058936 is the WIPO publication of the international application PCT/EP04/13664 (PCT '664) and the present application is the US national phase of PCT '664. None of the other polynucleotide sequences that appear on the search report encode the claimed *Secale cereale* c 4 allergens. To this end, the next top-matching sequence of AEB28059 (GenBank accession: AJ862833; GI:55859459; 90.7% identical to Applicants' polynucleotide of SEQ ID NO: 1) encodes a protein of 518 amino acids (GenBank accession CAH92633). The sequence identity between the Applicants' *Sec* c 4 protein of SEQ ID NO: 2 and the CAH92633 sequence (protein encoded by the DNA identified as result No. 2) at the protein level is 92% (39 mismatches). Similarly, the sequence identity between the Applicants' *Sec c* 4 protein of SEQ ID NO: 4

and the CAH92633 sequence at the protein level is 88% (60 mismatches). See the enclosed BLAST alignment results. Thus it is clear, at least based on the enclosed analysis, that the claimed *Secale cereale* c 4 polypeptides are both novel and unobvious over the art-known proteins.

It is by now well-established that "a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." See MPEP 52131 and further corroborated by the Fed. Circuit's decision in *VerdegaalBros. v. Union Oil Co. of Cal~brvia,* 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). With respect to inherency, the Courts have established that "the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.'" *In re Robertson,* 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999). Inasmuch as the cited Govorovic says nothing about *Secale cereale* c 4 polypeptide sequences and the Examiner has not established that the Sec c 4 polypeptide disclosed therein necessarily comprises the sequences recited herein, the rejection is without legal merit.

Applicants further submit that for anticipation, "the identical invention must be shown in as complete detail as is contained in the ... claim." *RJchardson v. Suzuki Motor Co.,* 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). The Office Action fails to establish that the polypeptides disclosed in the aforementioned reference contain the complete Sec c4 polypeptide sequence as presently claimed. To this end, Applicants find that a search of the term "Secale cereale sec c 4" in NCBI's protein database results in the identification of at least two Sec c 4 variants (accession Nos. CAH92630 and CAH92627) and an unrelated PEP carboxylase protein (accession No. AAS88378). It cannot be ascertained whether the reference teaches a sequence that is completely different from what is claimed in the present application. More importantly, it is clear that the cited reference of Gavorovic fails to provide "a complete detail" (i.e., the polypeptide sequence) of the claimed invention. As such, an inherency rejection under ~102/~103 is not supported and should be withdrawn. See MPEP 52112.

As an initial matter, claim 11 has been canceled, so it appears that Applicant is referring to claim 24's fragments in their argument. The "comprising" language in the claim parts (b) and (d) open up the claim to read on full-length SEQ ID NO:2 and SEQ ID NO:4.

Applicant's argument that the structural information of Gavrovic is inconsistent with SEQ ID NO:2 or SEQ ID NO:4 is unpersuasive. Applicant's argument that the Sec c 4 allergen of Gavrovic with a molecular weight of "about 55-60 kDa" and a pI "in range 9.2 to 9.7" is not the same was SEQ ID NO:2 or SEQ ID NO:4, with molecular weights of 57.172 kDa and 57.171 kDa and pI values of 9.08 and 9.28, respectively is not persuasive. 57.172 kDa and 57.171 kDa are both "about 55-60 kDa" and pIs of 9.08 and 9.28 are very much "in the range of 9.2 to 9.7."

Since the office does not have a laboratory to test the reference sequences, it is applicant's burden to show that the reference molecules differ from the claimed sequences. See In re Best, 195 USPQ 430, 433 (CCPA 1977); In re Marosi, 218 USPQ 289, 292-293 (Fed. Cir. 1983); and In re Fitzgerald et al., 205 USPQ 594 (CCPA 1980.

Applicant's arguments with respect to the USPTO sequence searches is not persuasive. Sequence searches performed at the USPTO are done in many different databases and the sequences themselves are searched in many different manners. Applicant has no way of knowing which sequences were searched, in what way the results were generated or displayed or in what databases the searches were performed. Therefore, Applicant's sequence search results arguments are without merit. Further, it is noted that sequence searches and results are imperfect, often incomplete and require the Examiner processing of the information. The Examiner uses the sequence searches as a tool to find relevant publications and information, but the sequence searches themselves are not evidentiary in nature.

Furthermore, Applicant's arguments with respect to the sequence search results would not be persuasive even if the sequence search results were sufficient evidence of all relevant art. As the Examiner argued in the previous Office Actions and *supra*, recitations of sequences in the claims add no patentable weight. Determining the sequence of the reference allergen is merely further characterization of a known compound. Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999). The same isolated Sec c 4 allergen was taught in the prior art of Gavrovic et al. Recitations of the sequence of SEQ ID NO:2 or SEQ ID NO:4 do not add patentability to the claims because it is only further characterization of a known compound.

Therefore, the rejection is maintained.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 12-13 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gavrovic et al. (PTO-892 mailed on 11/28/2008; Reference V) in view of U.S. Patent 5,762,943 (PTO-892; Reference A).

Gavrovic et al. has been discussed supra.

The claimed invention differs from the prior art in the recitation of "a medicament comprising at least one polypeptide according to claim 24 and a carrier" of claim 12 and "a pharmaceutical composition comprising at least one polypeptide according to Claim 24 and an active ingredient or an adjuvant " of claim 13.

U.S. Patent 5,762,943 teaches pharmaceutical compositions for treating type I hypersensitivity in a warm blooded animals sensitive to a pollen allergen (medicament) comprising an effective amount of a pollen allergen to which said warm blooded animal is sensitive, a refined detoxified endotoxin selected from the group consisting of monophosphoryl

lipid A and 3-deacylated monophosphoryl lipid A (active ingredients, adjuvants) and a pharmaceutically acceptable carrier (In particular, column 7, lines 18-21, claims 15-41, whole document).

It would have been obvious to one of ordinary skill in the art to use the Sec c 4 pollen allergen taught by Gavrovic et al. in the pharmaceutical compositions for treating type I hypersensitivity in a warm blooded animals sensitive to a pollen allergen comprising an effective amount of a pollen allergen to which said warm blooded animal is sensitive, a refined detoxified endotoxin selected from the group consisting of monophosphoryl lipid A and 3-deacylated monophosphoryl lipid A, and a pharmaceutically acceptable carrier taught by U.S. Patent 5,762,943 to treat type I hypersensitivity to Secale cereale pollen allergen Sec c 4.

From the reference teachings, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the reference, especially in the absence of evidence to the contrary.

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nora M. Rooney whose telephone number is (571) 272-9937. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by

telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

March 23, 2010

Nora M. Rooney

Patent Examiner

Technology Center 1600

/Nora M Rooney/

Examiner, Art Unit 1644